MUCOID SUBSTANCES AND CUTANEOUS CONNECTIVE TISSUE IN DERMATOSES

III. Cutaneous Mucopolysaccharides in Inflammation of the Skin*

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This study concerns observations on mucoid substances in the cutis in dermal inflammations, their localization in tissue sections stained after the periodic acid-Schiff-McManus method (PAS) and with toluidine blue, and their relationship to the various types of cutaneous connective tissue fibers.

The literature on the subject is rather sparse. Sylvén (17) did not obtain toluidine blue metachromasia which would indicate the presence of mucopolysaccharides in "banal", purulent and chronic inflammations. Asboe-Hansen (1) observed little metachromasia in edematous tissues—but marked, diffuse metachromasia in the corium of atopic dermatitis, and some metachromasia in contact type dermatitis, lichen simplex and lichen planus. In all of these diseases the metachromasia was hyaluronidase-susceptible.

With PAS, Stoughton and Wells (16) found no fuchsinophilic substances, i.e., polysaccharides, in numerous cases of eleven different, inflammatory skin diseases. In a number of cases of disseminated neurodermatitis, acne rosacea and toxic dermatitis there was PAS-positive "collagen" but these sections were from exposed skin in which the basophilic degenerative connective tissue stains red with PAS-fuchsin (3, 4, 10, 15, 16, 19). By contrast, Hollander, et al. (5), found increased PAS staining of the basal membranes, capillaries and "ground substance" in psoriasis, chronic eczema and lichen simplex. Braun-Falco (2) also observed increased PAS staining of basal membranes and vessels in different types of eczema and psoriasis, furthermore in vesicular and bullous eruptions and in lichen planus. The basal membranes appeared sometimes irregular, especially in areas of cutaneous infiltration and epidermal colliquation or vesiculation, e.g., in lichen planus and pemphigus. The reticulum was usually PAS-fuchsinophilic, and, like the basal membranes, metachromatic with toluidine blue. This metachromasia was, as a rule, hyaluronidase-labile. Observations on PAS stains of the basal membranes in eczema and dermatitis herpetiformis by Prunieras (13) were essentially in agreement with the descriptions of Braun-Falco (2).

The present findings were obtained in tissue material listed in Table 1. The histologic and histochemical methods used were the same as in previously reported studies on mucopolysaccharides in skin diseases (14).

OBSERVATIONS

There is little PAS staining in cutaneous inflammations. Three structures show increased or abnormal PAS-fuchsinophilia: The epidermal basal membranes, the papillae and subepidermal zones, and the inflammatory reticulum.

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TABLE 1

Material and results

Diagnosis	PAS Staining				Toluidine Blue beta metachromasia, hyaluronidase-fast	Elastic Degeneration
	Basement membranes		Subepidermal staining	Reticulum (increased)		
	thickened	irregular				
Acute eczema* (7)		+	+		+	
Chronic eczema* (10)	+			+	+−	+−
Psoriasis vulg. (8)	+			+	+−	+−
Parapsoriasis (3)		+				+
Lichen planus (4)	+			++	+−	+
Pityriasis rosea (1)		+				
Pemphigus vulg. (6)	+				+−	+−
Dermatitis herpetiformis (4)		+	+	+−	+	+
Erythema multiforme (1)		+	+		+	
Herpes Zoster (1)		+		+−		+−

* Types of "eczema": Contact type, nummular, infectious, seborrheic, lichen simplex, "chronic", erythroderma.

In acute eczemas, erythrodermias, parapsoriasis, pityriasis rosea and in vesiculo-bullous eruptions (except pemphigus) the epidermal basal membrances are irregular; sometimes they are thickened, sharply delineated, purple or red, in other places indistinct, diffuse and pink (fig. 1) or they are even entirely unstained and missing. Indistinct staining and lack of staining occur in areas of edema, basal cell liquefaction (fig. 1) or vesicle formation at the dermo-epidermal junction.

In chronic eczemas, lichen planus, psoriasis and pemphigus the basal membranes are either unchanged (fig. 2) or the red PAS stain is more pronounced than usual, i. e., the basal membranes are thickened.

In edematous lesions, e. g., in acute eczemas, dermatitis herpetiformis and erythema multiforme, the upper portions of the papillae and a narrow subepidermal zone show a diffuse, pink color (fig. 1).

Chronic eczemas, psoriasis, and lichen planus, i. e., chronic lesions in general, reveal distinct PAS staining of the infiltrative reticulum (figs. 2, 3). In psoriasis this is particularly pronounced in the papillae while in diffuse infiltrates, e. g., of lichen planus, the PAS-positive reticulum occupies the upper cutis throughout (fig. 2).

The toluidine blue metachromasia does not always correspond to the PAS-fuchsinophilia of the inflammatory tissues. There is never a red gamma metachromasis and not even the beta metachromasia is always distinct. The basal membranes show, for instance, often only little and indistinct toluidine blue staining. However, where a pronouncedly fuchsinophilic basal membrane is present, and in areas which show a diffuse PAS staining of the subepidermal zone there is also frequently a diffuse violet or pink toluidine blue metachromasia. The reticulum exhibits a violet or pink color with toluidine blue. However, this stain usually shows less of the reticulum than PAS.

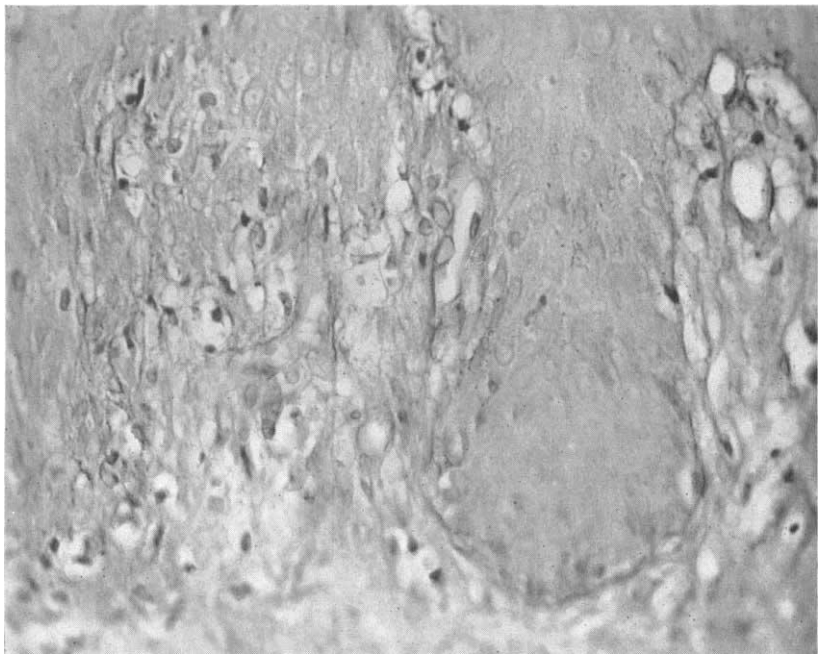

FIG. 1. Acute, nummular eczema. PAS stain. × 425 (Black-white picture × 385). Irregular, defective basal membrane, diffuse subepidermal PAS staining.

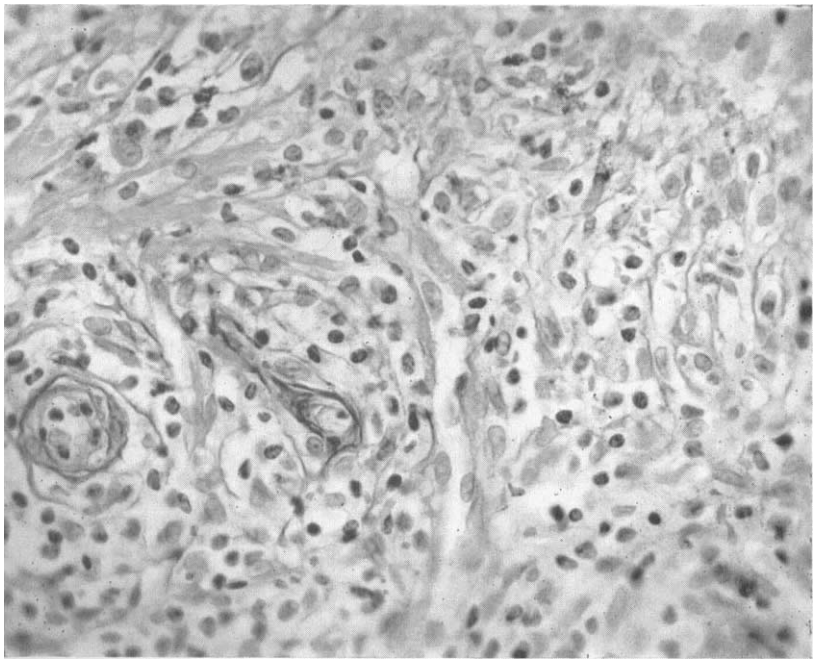

FIG. 2. Lichen planus. PAS stain. × 510. Fuchsinophilic reticulum fibers quite well stained.

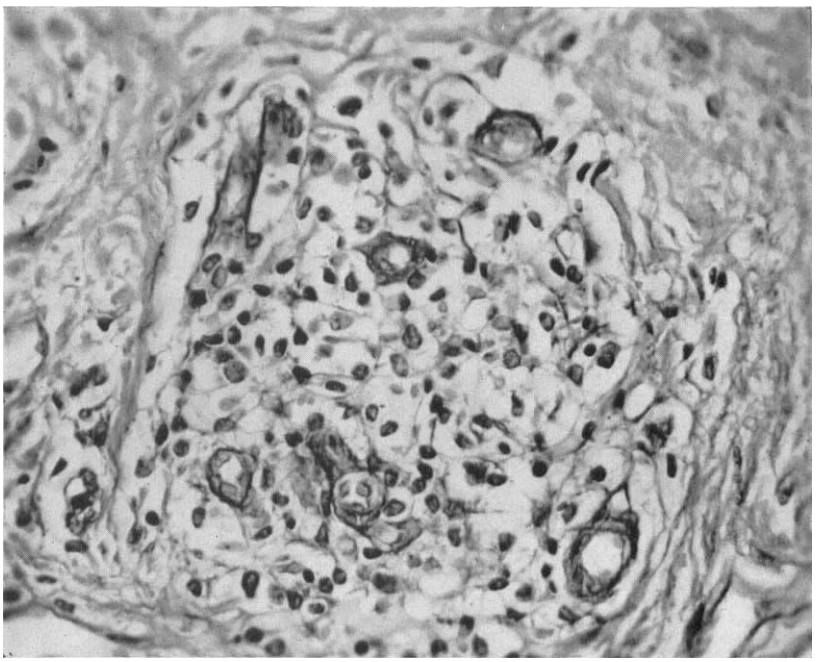

FIG. 3. Chronic contact type eczema. PAS stain. × 500. Fuchsinophilic reticulum in an inflammatory papilla cut almost parallel to the surface.

Pre-treatment with testicular hyaluronidase has no effect on PAS staining or toluidine blue metachromasia of inflammatory lesions.

A comparison of PAS and silver stains reveals a fairly good presentation of the argyrophilic network with the PAS method. The reticulum is poorly or at best only moderately developed in acute eczema, parapsoriasis, erythema multiforme and pemphigus. It is prominent, as a rule, in chronic eczemas, lichen planus, dermatitis herpetiformis and herpes zoster. In lichen planus, particularly, there is an abundant reticulum. In psoriasis the extent of the reticulum depends on the degree of infiltration. This applies quite generally, also to other inflammations. The argyrophilic network is prominent wherever there is much infiltrate regardless of acuteness or chronicity, edema or vesiculation of the lesions.

There is no correlation between PAS-stained structures and elastic tissue; no fuchsinophilic or metachromatic elastic fibers can be found. In diffuse infiltrates and chronic lesions the elastica tends to fragment and to become atrophic. It appears, therefore, more damaged in lesions in which there is a prominent reticulum. On the other hand, in some instances the elastic tissue appears unaltered although a distinct reticulum is present (e.g., in seborrheic dermatitis).

COMMENTS

Chronic inflammatory diseases of the skin, e.g., chronic eczema, psoriasis, lichen planus, show some excess of mucopolysaccharides. This observation conforms with the reports of most of the previous investigators (1, 2, 5, 13). The

epidermal basal membranes, in particular, are often thickened and pronouncedly fuchsinophilic. The findings are at some variance with those obtained by Stoughton and Wells (16) inasmuch as these investigators did not observe thickening of the basal membrane as an attribute of various inflammations, and they regarded the thickening in lupus erythematosus as characteristic of that disease.

As was noted by others (2, 13), acute inflammations often show defects of the basal membrane in areas of edema or vesiculation. In view of an increase in local hyaluronidase in some of these lesions, it is possible that the disintegration of the PAS-positive basal membrane is due to an abnormal hyaluronidase content of the edema or vesicle fluid.

The positive PAS stain of the reticulum is characteristic for normal argyrophilic fibers (2, 6, 7, 8, 14, 20). The extent of the reticulum, described in many diseases by previous observers (2, 12, 18) is well outlined by PAS. Way (18) mentioned an extensive reticulum in eczema, and a moderately developed argyrophilic network in lichen planus. In the latter disease, however, the reticulum seems more prominent than described by Way (18). It is actually comparable to the most pronounced types of reticulum which occur in pleomorphic lymphoblastomas, e.g., mycosis fungoides (12, 14, 18). In contrast to many other skin diseases (tumorous infiltrations, collagen diseases, basophilic degeneration (14, 15), there are, in inflammatory skin diseases, generally no morphologic or tinctorial abnormalities of the argyrophilic fibers.

Degeneration of the elastic tissue in inflammation has been described by many observers; e.g., Percival, et al. mentioned the absence of elastic fibers in erythrodermas (12)—and Winer observed that elastic tissue is less resistant to inflammation than collagen (19).

The nature of the mucoid material which is present in excess in the inflammatory tissues has been identified as mucoprotein by beta metachromasia with toluidine blue and by hyaluronidase-fastness (9, 11). No free acid mucopolysaccharides occur in inflammatory cutaneous lesions.

SUMMARY

1. The mucopolysaccharides of inflammatory cutaneous lesions are slightly increased above the normal. They are characterized as mucoproteins by their PAS-fuchsinophilia, by beta metachromasia with toluidine blue and by hyaluronidase fastness.

2. The mucoids are more increased in chronic inflammations than in acute processes. They are located in the basal membrane, just below the epidermis, and in the reticulum. In many of the chronic inflammations, increased PAS staining of the basal membrane reveals a thickening of the membrane.

3. Defects of the basement membranes combined with diffuse subepidermal PAS staining occur in edematous and vesicular lesions. They are perhaps due to the action of increased tissue hyaluronidase.

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